REMARKS

At page 11 of the Response filed on June 11, 2003, Applicants indicated that they are currently in the process of preparing a Declaration Under 37 CFR 1.132 in order to provide evidence of the absence of the 1350 dalton biopolymer marker(amino acid residues 2-14 of SEQ ID NO:1) in normal (non-diseased) human sera and will forward this Declaration to the Examiner as soon as it is complete. Applicants also indicated that they will further address the rejection under U.S.C. 112, first paragraph at the time the Declaration is submitted.

The Declaration Under 37 CFR 1.132 is now complete and is submitted herewith. The rejection under 35 USC 112, first paragraph presented in the Office Action mailed on March 11, 2003 is addressed below.

Rejection under 35 USC 112, first paragraph

Claims 3-9, 18-28 and 33-35, as originally presented, stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which allegedly was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or which with it is most nearly connected, to make and/or use the invention.

The Examiner asserts that claims 3-9, 18-28 and 33-35 are broadly drawn to methods of determining the presence or absence of

myocardial infarction or renal failure by analyzing a biological sample obtained from a patient to identify the biopolymer marker sequence consisting of SEQ ID NO:1. The Examiner also asserts that the specification contemplates the use of these methods for diagnosing, staging, monitoring, prognosticating or determining predisposition to myocardial infarction or renal failure; the diagnostic methods include, for example, biopolymer evidencing, characterization, regulation, risk-assessment and therapeutic identification.

Claims 3-9, 18-28 and 33-35 have been canceled. The remaining pending claims are now limited to methods and kits using a specific biopolymer marker peptide (amino acid residues 2-14 of SEQ ID NO:1) specifically diagnostic for myocardial infarction or renal failure. The diagnostic methods of the remaining pending claims determine that the presence of amino acid residues 2-14 of SEQ ID NO:1 identified in a biological sample (bodily fluid or tissue sample) obtained from a patient is a positive indicator of myocardial infarction or renal failure. The kits of the remaining pending claims are used to carry out the claimed specific diagnostic methods for myocardial infarction or renal failure. Applicants respectfully draw the Examiner's attention to the fact that methods and/or kits involving staging, monitoring, prognosticating, determining predisposition to, evidencing, characterization and regulating myocardial infarction or renal failure are not claimed

in the instant invention. Additionally, methods and/or kits involving risk-assessment, therapy and therapeutic identification as related to myocardial infarction or renal failure are not claimed. Applicants are not required to enable material that is not claimed (see MPEP 2164.08).

The Examiner further asserts that it is not clear how the biopolymer marker will be utilized to distinguish the two unrelated disease states. In other words how will one identify myocardial infarction from renal failure. The Examiner asserts that the specification does not enable one of ordinary skill in the art to definitively assess the incidence or further distinguish between both diseases in a single test sample. Applicants do not claim the ability to assess the incidence of or further distinguish between both diseases in a single test sample, nor are Applicants claiming the ability to distinguish between myocardial infarction and renal failure. As is stated above, Applicants are not required to enable material that is not claimed (see MPEP 2164.08).

Additionally, applicants are not required to explain the disease process of myocardial infarction or renal failure, applicants are only required to show that the claimed peptide is indicative of myocardial infarction and renal failure (see MPEP 2165.03). Applicants state an aim of the invention at page 5, lines 7-11 of the instant specification, "The instant inventors do not attempt to develop a reference "normal", but rather strive to

specify particular markers which are evidentiary of at least one particular disease state, whereby the presence of said marker serves as a positive indicator of disease". Applicants claim that the presence of the biopolymer marker peptide (amino acid residues 2-14 of SEQ ID NO:1) in a biological sample obtained from a patient is a positive indicator of myocardial infarction and renal failure. Figure 1 shows the results of experiments wherein amino acid residues 2-14 of SEQ ID NO:1 was identified in biological samples obtained from patients having a history of either myocardial infarction or renal failure; thus Applicants claim is enabled by the original disclosure.

Applicants assert that the instant specification teaches those of skill in the art how the claimed peptide was isolated and identified without undue experimentation and further assert that the instant specification sets forth a protocol which can be followed to isolate and identify biopolymer markers of any disease condition. Pages 20-27 of the instant specification provide specific steps and protocols one would carry out to identify the claimed biopolymer marker peptide. Furthermore, the chromatographic and mass spectrometric techniques used in the protocols of the instant invention are well-known to those of skill in the art. Thus, one of skill in the art would be familiar with the techniques used and would know how to carry out the protocols in the instant disclosure. Alternatively, if one of skill in the art did not know

exactly how to carry out the protocols in the instant invention, one of skill in the art would know where to locate the information in the prior art since the techniques used in the instant disclosure are well-described in the art. Applicant is not required to describe what is well known in the art. A patent need not teach, and preferably omits, what is well known in the art (see MPEP 2164.01).

According to the methods of the instant invention; a biological sample(page 28,line 11 to page 29,line 7 refers to the use of various types of samples and their measurement) is obtained from a patient(figure 1 shows data derived from patients) and first treated with one of the chromatographic protocols described on pages 20-25. The sample is then subjected to treatment with mass spectrometric techniques in order to identify the peptides present within the sample. The resulting spectral profiles of the peptides present in the sample are compared to spectral profiles of known peptides. The peptides within the sample are further verified by comparison of their sequences to known sequences recorded in databases. One of skill in the art would recognize that the method described in the instant paragraph can be followed to identify biopolymer markers of any disease condition.

However, the Examiner asserts that the results obtained from the method which are set forth in figure 1, are not clearly indicative of myocardial infarction and renal failure because no

control sample analysis is presented by way of example.

In response to this assertion, Applicants herein provide the attached Declaration (including one figure) under 37 CFR 1.132. The figure attached to the declaration provides side-by-side profiles (obtained using techniques of mass spectrometry) of healthy (normal) human sera versus sera from a patient having a history of myocardial infarction. This profile comparison clearly evidences the absence of the 1350 dalton marker in normal human sera and thus establishes the specificity of the 1350 dalton peptide as a marker which when present in the sera is diagnostic for myocardial infarction. This figure does not represent results obtained from additional experimentation. The profiles were reproduced from data obtained in the original experiments performed at the time of the invention.

The Examiner further asserts that while the evidence presented in the specification does point to the high occurrence of the sequence in both myocardial infarction and renal failure, this is not sufficient in implementing the said sequence in a molecular based diagnostic method for both myocardial infarction and renal failure with said sequence. Applicants claim that the presence of amino acid residues 2-14 of SEQ ID NO:1 in the sera of a patient is indicative of myocardial infarction or renal failure and enable this claim both by description of the procedures used to isolate and identify amino acid residues 2-14 of SEQ ID NO:1 in the

specification and by example in the data shown in Figure 1.. Applicants respectfully assert that this is enough to enable the claimed marker for diagnostic purpose in myocardial infarction and renal failure.

The Examiner additionally asserts that Applicants have not provided any disclosure enabling the use of the biopolymer marker with regard to regulating the presence or absence of said sequence. Applicants have not claimed the ability to regulate the presence or absence of amino acid residues 2-14 of SEQ ID NO:1; Applicants observe the presence of amino acid residues 2-14 of SEQ ID NO:1 in biological samples obtained from patients. Furthermore, as stated above, Applicants are not required to enable material that is not claimed (see MPEP 2164.08).

The Examiner states that there is no disclosure designating how the sequence bound in the method that could be regarded as enabling one of ordinary skill in the art to use the said sequences in the diagnostic method. Applicants have shown by the description of methods set forth in the specification and exemplified by data in Figure 1 that the presence of amino acid residues 2-14 of SEQ ID NO:1 is a positive indicator of myocardial infarction and renal failure. Applicants respectfully submit that one of ordinary skill in the art after reviewing the specification and the declaration filed herewith would know how to use the claimed biopolymer marker peptide (amino acid residues 2-14 of SEQ ID NO:1) to diagnose

myocardial infarction and renal failure.

The Examiner asserts that applicants have not set forth any supporting evidence that suggests that amino acid residues 2-14 of SEQ ID NO:1 is a unique molecular marker for myocardial infarction and renal failure. Again, this assertion of the Examiner requests enablement for information that is not claimed, as applicants are not claiming amino acid residues 2-14 of SEQ ID NO:1 to be a unique molecular marker of myocardial infarction, renal failure or any other disease condition.

The Examiner cites two articles; Tascilar *et al.* (Annals of Oncology 10, Supplement 4:S107-S110 1999) and Tockman *et al.* (Cancer Research 52:2711s-2718s 1992) which are allegedly relevant to the instant invention. The Examiner did not provide a copy of the article by Tascilar *et al.* with the Office Action mailed on March 11, 2003, thus the article will be addressed in this response only with reference to what is written in the Office Action about the article.

According to the Examiner, Tascilar *et al.* is an article published in an oncogenic journal reporting on diagnostic methods in the realm of disease states. The Examiner appears to have drawn a direct parallel between the diagnostic methods reported by Tascilar *et al.* and the diagnostic methods of the instant invention. The Examiner then cites two fragmented quotations from Tascilar *et al.* "...these tests should be interpreted with

caution..." and "the genetic changes found in sources other than the pancreas itself (blood, stool) should be evaluated prudently". Although it is difficult to clearly ascertain intended meaning from fragmented quotations presented out of context, the Examiner appears to be commenting on the predictability of molecular-based assays. Applicants claim that the presence of amino acid residues 2-14 of SEQ ID NO:1 is a positive indicator of myocardial infarction or renal failure; a statement which is enabled by the description of methods as set forth in the specification and by data presented in Figure 1. Thus, applicants respectfully submit that the claimed method involves a simple observation of the presence of amino acid residues 21-4 of SEQ ID NO:1 (as shown in Figure 1) and does not require any other evaluation of genetic changes in the organism in which the sequence is observed. Thus, it is respectfully submitted that the Tascilar *et al.* article is not relevant to the instant invention.

Tockman *et al.* is deemed to teach conditions necessary for a suspected cancer biomarker (intermediate end point marker) to have efficacy and success in a clinical application. The reference is drawn to biomarkers for early lung cancer detection, however the basic principles are applicable to other oncogenic disorders, according to the Examiner. Tockman *et al.* is deemed to teach that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end

points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials. Early stage markers of carcinogenesis have clear biological plausiblity as markers of pre-clinical cancer if validated to a known cancer outcome. Tockman *et al.* is deemed to teach that the essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical disease and link those marker results with histological confirmation of disease.

The first thing noted about the Tockman *et al.* reference is the publication date; it was published almost ten years prior to the date of Applicants' invention. Theories and standards in biotechnology change quickly over time and especially over a decade. Thus, the Tockman *et al.* reference is not considered to accurately assess the field of the invention at the time of Applicants' invention.

The Tockman *et al.* article is concerned with early detection of cancer biomarkers and apparently does not discuss biomarkers for myocardial infarction and renal failure. Although both the Tockman *et al.* reference and the instant invention are drawn to the identification of biomarkers, they are not considered to be analogous since a direct parallel can not be drawn between the neoplastic disease process and the disease process of myocardial infarction and renal failure . The Tockman *et al.* reference is

further not analogous in the type of markers taught. Tockman *et al.*. discusses biomarkers for early detection of disease wherein in order to a show a marker for early detection the marker must be present before standard clinical diagnosis of the disease. Applicants identify the claimed biomarker (amino acid residues 2-14 of SEQ ID NO:1) in the serum of patients with a history of myocardial infarction or renal failure. Applicants are not claiming the marker to be present before the development of myocardial infarction or renal failure, thus it is not necessary to link or validate the marker with confirmation of disease.

Furthermore, Applicants do not claim the marker to have any predictive value, thus there is no need to confirm marker predictive value in population trials.

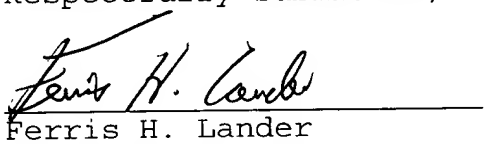
Based on the considerations noted in the above paragraphs, it is respectfully submitted that the Tockman *et al.* article is not relevant to the instant invention.

Accordingly, as demonstrated in the above-discussion, Applicants assert that one of ordinary skill in the art when reviewing the instant specification and declaration filed herewith would recognize how to use the claimed peptide as a marker for myocardial infarction or renal failure. Thus, Applicants respectfully request that this rejection under 35 U.S.C. 112, first paragraph now be withdrawn.

CONCLUSION

In light of the Response filed on June 11, 2003 and the remarks and Declaration Under 37 CFR 1.132 submitted herewith, it is respectfully submitted that the Examiner will now find the claims of the application allowable. Favorable reconsideration of the application is courteously requested.

Respectfully submitted,



Ferris H. Lander
Registration # 43,377

McHale & Slavin, P.A.
2855 PGA Boulevard
Palm Beach Gardens, FL 33410
(561) 625-6575 (Voice)
(561) 625-6572 (Fax)

\\Ns2\DRV_E\STAFF DATA FILES\Ferris Lander's Files\FL\AMENDMNT.PAT\2132_031_SupplAM1.wpd